REMARKS

Claim 1, the only claim pending in the application, is as follows:

> 1. A congenic rat comprising a mutant GPR10 gene, wherein said congenic rat is obtained by crossing a Otsuka Long-Evans Tokushima Fatty (OTELF) rat (ATCC No. 72016) with a wild-type rat, and wherein said congenic rat exhibits a prolonged immobilization time when assayed in a forced swim test compared to said wild-type rat and anti-anxiety behavior in a elevated plus-maze test compared to said wild-type rat.

As described for example at page 1, lines 1-11 of the specification, the claimed congenic rat displays depression-like and anti-anxiety-like behavior, and is thus useful as a model of depression and anxiety.

I. "Specific, Substantial, and Credible Utility"

As described in the MPEP at sections 2107.01-.02, the examination guidelines require that an invention have a specific and substantial utility that is credible.

A **"specific"** utility is specific to the claimed subject matter, as opposed to being applicable to the general subject matter of the invention. For example, the claimed congenic rat is particularly useful as a model of depression and/or anxiety, as compared to other rats. This is certainly a specific utility.

A "**substantial**" utility is a "real-world" use. Screening compounds useful for treating depression and/or anxiety is certainly a real-world use.

An asserted utility is presumed ***"credible"*** unless (A) the logic underlying the assertion is seriously flawed, or (B) the facts upon which the assertion is based are inconsistent with the logic underlying the assertion. Generally, an asserted utility is presumed credible unless a person of ordinary skill in the art would consider the assertion to be incredible in view of contemporary knowledge.

Under the current examination guidelines, "[w]here an Applicant has specifically asserted that an invention has a particular utility, that assertion cannot simply be dismissed by Office personnel as being 'wrong,' even where there may be reason to believe that the assertion is not entirely accurate. See MPEP at Section 2107.02(III)(B).

The Examiner's comments during prosecution of this case relate to the *credibility* of Applicants' asserted utility. While at times the Examiner attempts to cast the issue as one of a "specific" utility, or one of a "substantial" utility, it is believed that this is inconsistent with the examination guidelines. The Examiner's comments are at best relevant to the issue of credibility.

II. Examiner's Rejection of Claim 1 Under 35 USC §101/112

As set forth in the May 3, 2005 Office Action, claim 1 is rejected as lacking patentable utility. Because the basis for the Examiner's conclusion appears to change with each office communication, a brief summary of the prosecution history is set forth below.

Non-Final Office Action Dated November 12, 2004 and Applicants' Response Thereto

In the first Office Action, the Examiner stated that:

> [t]he specification discloses that [the] congenic rat of the invention can be used as a model for treating psychiatric diseases such as depression. While this utility ***is specific*** to the congenic rat of the invention, ***it is not a credible utility*** as a model of human disease. The reason this is not a credible utility is because human depression has not been linked to mutations in GPR10.... Taken together in humans, mice and rats the mutations in GPR10 have disclosed different phenotypes." (See Non-Final Office Action at pages 14 and 15) (emphasis added)

Further, the Non-Final Office Action stated at pages 16-17: "The specification discloses that ***the congenic rat of the invention exhibit significant depression***...but fails to disclose any correlation to humans with depression or to humans with GPR10 mutation." (emphasis added)

In Response, Applicants established that the art does not suggest that mutations in GPR10 manifest as different phenotypes in mice, rats and humans, and thus, the claimed rat has a credible utility as a model for human depression and/or anxiety.

Final Office Action Dated May 3, 2005, and Applicants' Response Thereto

In the Final Office Action, the Examiner maintained the utility/enablement rejection "for reasons set forth in the Office Action mailed November 12, 2004" (see page 2 of the May 3, 2005 Office Action). The Examiner concluded in the Final Office Action that mutations in GPR10 are manifested as different phenotypes in humans, mice and rats, and thus the claimed congenic rat lacked a "***specific***" utility. (see page 3 of the Final Office Action)

In Response, Applicants again established that the art does not suggest that mutations in GPR10 are associated with different phenotypes in mice, rats and humans, and thus, the claimed rat has a credible utility. Further, Applicants asserted that using the claimed rats, which display useful phenotypes related to depression and/or anxiety, as a model of depression and/or anxiety was a "specific" utility.

Advisory Action Dated July 15, 2005

In an Advisory Action, the Examiner admitted that the claimed congenic rat has a "credible" utility, but contended that the congenic rat does not have a "specific and substantial" utility for reasons that were *not* specified. The Examiner further contended that the specification was not enabling for claim 1, because the specification does not show that GPR10 is associated with depression.

Personal Interview Conducted on July 28, 2005

In order to clarify the Examiner's position, a personal interview was conducted between the Examiner and the undersigned. During the interview, the Examiner clarified that the utility and enablement rejections were coextensive, and requested that Applicants establish that the recited phenotypes of the claimed congenic rat correlate to depression and/or anxiety, and that the recited forced swim test and elevated plus-maze test are known in the art for assessing depression- and/or anxiety-like behavior in the rat (see Examiner's Interview Summary).

Applicant's Second Response to the Final Office Action

In a Second Response to the Final Office Action, Applicants submitted literature evidence demonstrating that, indeed, the forced swim test and the elevated plus-maze test

(recited in claim 1) are well-known assays for screening antidepressant drugs and anxiolytic drugs in the rat, and are well-known for assessing depression-like and anxious-like behavior in rats.

Advisory Action Dated November 11, 2005

In the second Advisory Action, the Examiner admitted that the literature evidence submitted by Applicants addresses wild-type rats as models of depression. However, the Examiner contends that the evidence is insufficient to overcome the section 101 rejection because the literature does not address the use of *congenic* rats in these assays. Specifically, the Examiner contends that one of the eight references submitted by Applicants (Pellows et al.) allegedly indicates that strain is an important factor in the elevated-plus maze test.

The Examiner concludes that Pellows et al. supports a conclusion that the disclosed phenotype of the claimed congenic rat may be due to the *strain* and not to the mutant GPR10 gene.

III. Applicants Further Response to the Utility/Enablement Rejection

Initially, the Examiner is requested to note that the phenotype of the claimed congenic rat is characterized by *two* tests known for assessing depression-like and/or anxiety-like symptoms in rats, the forced-swim test and the elevated plus-maze test. The Examiner's comments do not address the forced swim test, which also clearly establishes the effect of the mutation on the rat's behavioral phenotype.

With respect to the elevated-plus maze test, the passage of Pellows et al, to which the Examiner refers in the Advisory Action, is as follows:

> Our experiments with different rat strains showed that in principle both hooded and albino strains are suitable for this procedure (this is not the case, for example, with the social interaction test...). However, in the course of pilot studies we found one strain of hooded rat that lacked consistent aversion to the open arms; these were black hooded PVG rats from Banting and Kingman, U.K. Clearly, therefore, the selection of a suitable strain is important. We selected Olac rats for our other studies, and although the percentage of open arms entries showed some variation between the different control groups, this was not too marked and ranged from 20-40%. Pellow et al., *J. Neurosci. Methods* 149-167 (1985).

The Examiner's comments in the Advisory Action, that the disclosed phenotype of the rat may be due to genetic differences other than the GPR10 mutation, are based on a misunderstanding regarding the identity of the wild-type rat used in both the forced swim test and the elevated plus-maze test of Examples 4 and 5 of the specification. The Examiner's attention is kindly directed to the specification at the paragraph bridging pages 7 and 8, describing the creation of the claimed congenic rat, along with Example 3 and Figure 12.

As is described in the specification, the genetic backgrounds of the congenic -/- rats (the claimed GPR10 mutant rat) and the control +/+ rats are not different, as the Examiner believes. As stated at page 3, lines 14-16, of the specification: "In the present invention, a congenic rat has been produced by introducing the mutant GPR10 (OLETF type) domain into the BN background." At page 7 of the specification, lines 24-26, the BN rat is described as a suitable wild-type rat.

More specifically, as shown in Fig. 12 and described in Example 3, the congenic -/- rats were produced by mating heterozygous (-/+) parent rats, which allows one to obtain the control +/+ rats at a common generation. In fact, in Examples 4 and 5, the inventors assessed the phenotype of the -/- congenic rat relative to control +/+ rats from the same generation, both being born from heterozygous (-/+) parent rats.

Thus, in view of the present specification, one of ordinary skill in this art would understand that the behavioral difference of the claimed congenic rat in the elevated plus-maze test (Example 5), as compared to the wild-type control rat, is not due to a difference in genetic background (i.e. to strain), but is due to the claimed GPR10 mutation.

IV. Conclusion

In view of the above, and in view of Applicants' previous Responses, Applicants respectfully submit that:

(1) Using the claimed congenic rat as a model of depression and/or anxiety to screen for compounds useful in treatment ***is a specific and substantial utility***;

(1) GPR10 is not known to manifest different symptoms in humans, mice and rats (see Amendment filed March 10, 2005 and June 23, 2005), and thus the asserted utility is ***credible***;

(2) The elevated plus-maze test and forced-swim test are well-known assays for assessing depression-like and anxiety-like behavior in rats (see Response filed September 30, 2005), and thus, again, the asserted utility is ***credible;*** **and**

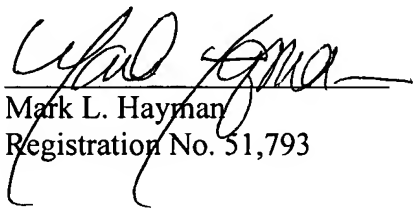
(3) The behavior of the congenic rat of the present invention was assessed in the elevated plus-maze test and the forced-swim test relative to wild-type rats ***having the same genetic background***. Thus, the asserted utility is ***credible.***

Therefore, the claimed congenic rat is useful as a model for human depression and/or anxiety, and such is a patentable utility. Accordingly, withdrawal of the Section 101/112 rejection is respectfully requested.

Further, as such is the only rejection outstanding, reconsideration and allowance of this application are now believed to be in order, and such actions are hereby solicited. If any points remain in issue which the Examiner feels may be best resolved through a personal or telephone interview, the Examiner is kindly requested to contact the undersigned at the telephone number listed below.

The USPTO is directed and authorized to charge all required fees, except for the Issue Fee and the Publication Fee, to Deposit Account No. 19-4880. Please also credit any overpayments to said Deposit Account.

Respectfully submitted,



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